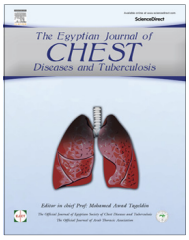
Egyptian Journal of Chest Diseases and Tuberculosis (2015) **64**, 793–797

HOSTED BY

The Egyptian Society of Chest Diseases and Tuberculosis

Egyptian Journal of Chest Diseases and Tuberculosis

www.elsevier.com/locate/ejcdt
www.sciencedirect.com



ORIGINAL ARTICLE

Using streptokinase for pleural adhesiolysis in sonographically septated pleural effusion

Amany Omar, Abd-Elazim Abo Elfadl, Yousef Ahmed *, Sahar Refaat

Chest Department, Assiut University, Egypt

Received 4 April 2015; accepted 22 June 2015
Available online 8 August 2015

KEYWORDS

Septated effusion;
Streptokinase;
Pleural adhesiolysis

Abstract *Background:* In dealing with septated pleural effusion, intrapleural fibrinolytics may be a useful alternative for others such as use of video assisted thoracic surgery or the conventional thoracotomy. The use of intrapleural fibrinolytics may be a safer, easier and cost effective management option that can promote pleural fluid drainage.

Objective: To evaluate the role of intrapleural streptokinase as a fibrinolytic agent in the management of pleural effusion with adhesions.

Patients and methods: This study was designed as a case series study in a prospective manner. Twenty-five patients were included in the study. All were admitted at Chest Department, Assiut University Hospital .The study was conducted during the period between September 2013 and September 2014. All patients had septated pleural effusion; candidate for drainage with failure of satisfactory pleural fluid drainage 24 h following intercostal tube (ICT) placement provided that the tube was properly positioned and not obstructed. Streptokinase was given daily at a dose of 250,000 IU dissolved in 40 ml of normal saline instilled in the pleural cavity through the chest tube. Instillation was repeated as long as no serious complication occurred and the drained fluid volume was >100 cc with a maximum of 14 doses. Patients were assessed by the amount of drainage through intercostal drain, chest X-ray and chest ultrasound. Also patients were assessed carefully for evidence of complications.

Results: The study revealed increased drainage of pleural fluid through intercostal tube after streptokinase instillation. The observation difference in fluid volume before and after streptokinase instillation is found to be highly significant statistically ($p < 0.001$) .Outcome was defined according to scoring of changes in X-ray and ultrasound with success rate of 60%. Chance of success increases when the adhesions are fine based on the sonographic features. No major adverse effects were noted.

Conclusion: We conclude that intrapleural streptokinase therapy may be considered in septated pleural effusion as a safe and effective treatment; it may obviate the need for surgery.

Also, the ultrasound echo features of adhesions could be considered as a predictor for the response.

* Corresponding author.
Peer review under responsibility of The Egyptian Society of Chest Diseases and Tuberculosis.

http://dx.doi.org/10.1016/j.ejcdt.2015.06.009

Introduction

Septated pleural effusions are those with ultrasound evidence of fibrin strands or septa floating inside the pleural space [1]. Intrapleural adhesions and septated effusions remain a common and burdensome clinical entity. The presence of adhesions carries a poor prognostic factor in patients with exudative pleural effusions and may render the pleural fluid drainage difficulty [2]. In dealing with this problem, intrapleural fibrinolytics may be a safe, easy, cost effective management option. Also, it may be a useful alternative for others such as use of video assisted thoracic surgery or the conventional thoracotomy [3]. The purpose of our study was to assess the safety and efficacy of streptokinase (SK) for intrapleural fibrinolysis in patients with septated pleural effusion.

Patients and methods

This study was designed as a case series study in a prospective manner. Twenty-five patients having septated pleural effusion were included in the study. All were admitted at Chest Department, Assiut University Hospital .The study was conducted during the period between September 2013 and September 2014.

Inclusion criteria

Patients who fulfilled all of the following criteria were included:

1 – Patient had pleural effusion with known underlying etiology.
2 – Presence of intrapleural adhesions as documented sonographically.
3 – Pleural fluid drainage was indicated.
4 – Difficult thoracentesis.
5 – Failure of satisfactory pleural fluid drainage 24 h following intercostal tube (ICT) placement provided that the tube was properly positioned and not obstructed.
6 – Patient agreed to contribute in this study.

Exclusion criteria

Patient was excluded from this study if one of the following was met:

1 – Recent severe trauma, hemorrhage, or stroke.
2 – Patient had bleeding disorder.
3 – Patient maintained on anticoagulant therapy.
4 – Patient had history of streptokinase (SK) administration in the previous 2 years.

The following were done before starting the treatment protocol

1 – A full history was taken and clinical examination was performed.
2 – Coagulation profile.
3 – X-ray and ultrasound evaluation of the chest.

Treatment protocol

All patients initially had a closed I.C.T drainage with a size 24–32 Fr. The chest tube is placed under the water seal system. The first dose of fibrinolytic therapy started 24 h after ICT placement. For intrapleural fibrinolysis, no premedications or analgesics were administered systemically or intrapleurally. Streptokinase was used at a dose of 250,000 IU dissolved in 40 ml of normal saline instilled in the pleural cavity through the chest tube. Patient was placed in the lateral decubitus position with the unaffected lung dependent during agent instillation, to be sure that all of this agent drained from the chest catheter into the treated pleural cavity. The tube is then clamped for 2–4 h and patient asked to repeatedly change position so that streptokinase could thoroughly spread in pleural cavity. Patient remained in bed until the tube was unclamped, to minimize the amount of agent that might leak out around the tube thereby decreasing its effective dwell time in the pleural cavity. Our plan during protocol application was to stop further instillation if severe complication occurred and if drained fluid through the tube was < 100 cc in 24 h provided that tube is patent and properly positioned. Also, we planned to continue the daily instillation as long as the drained fluid volume is > 100 cc with a maximum of 14 doses according to Maskell et al. [4]. Data about Volume of pleural fluid drained from the chest tube before and after streptokinase instillation were collected daily. Chest X-ray and chest ultrasound were performed daily till discharging day. Total dose of SK and number of instillations during the course of therapy were recorded.

The effectiveness of the protocol was assessed by

1 – Monitoring the volume of fluid drained from the chest tube daily.
2 – Chest ultrasound to check dissolution of adhesions.
3 – Chest radiography to see radiological clearance.

Evaluation of pleural effusion on discharging day by chest X-ray was described as

0 – No change.
1 – Less than 1/3 improvement.
2 – Improvement between 1/3 and 2/3.
3 – More than 2/3 improvement without complete clearance.
4 – Complete radiological clearance.

Regarding the evaluation by chest US, four results were recorded on discharge

0 – No change.
1 – Dissolution of adhesions in some regions.
2 – Dissolution of adhesions in all regions with residual pleural lesion.
3 – Total adhesion dissolution without residual pleural lesion.

Residual pleural lesion means pleural fibrosis, nodules or masses.

Outcome definition

Three groups were defined regarding the study outcome:

Failure: Chest X-ray scoring 0, and chest ultrasound scoring 0.
Partially successful: Chest X-ray scoring 1 or 2 and chest ultrasound scoring 1.
Successful: Chest X-ray scoring 3 or 4, and chest ultrasound scoring 2 or 3.

Patients addressed as failure or partially successful were transferred to cardiothoracic surgeon to select the suitable line for surgical interference. While in successful group the intercostal tube is removed and patient is discharged to continue their treatment according to the underlying etiology.

Complications assessment

Patients were assessed carefully for evidence of drug complications including fever, pain, allergic reaction, bleeding or hemodynamic changes. Fever was defined as a temperature greater than 38″C, or one degree elevation over baseline in previously febrile patients [5].

Statistical analysis

Categorical variables were described by number and percent (*No*, %), where continuous variables were described by mean and standard deviation (Mean, SD). *T*-test was used to compare between volume drained before and after streptokinase in studied patients. A two-tailed $p < 0.05$ was considered statistically significant. All analyses were performed with the SPSS 20.0 software.

Results

25 patients were included in the study (16 males and 9 females) with age ranging from 31 to 75 years and their descriptive data are demonstrated in Table 1.

Regarding the underlying etiology in studied patients the commonest cases we faced were empyema and parapneumonic effusion and the least common was clotted haemothorax as demonstrated in Table 2.

Table 3 shows that the amount of fluid drained increased after streptokinase by a mean value of 1061.6 and there is a significant statistical difference between drained fluid before and after instillation ($p < 0.01$).

The final outcome of the studied patients was defined based on the scoring of changes in X-ray and ultrasound on discharge. Patients were divided into successful, partially successful and failure groups. 60% of cases were successful as seen in Fig. 1.

In successful group the total used dose of streptokinase ranged from 1,250,000 IU to 3,000,000 IU which is the maximum dose we needed in our study (Table 4).

Sonographic echo features of pleural adhesions among different outcome groups are shown in Table 5. Chance of success increases when the adhesions are fine.

Table 1 Descriptive data of the studied patients ($n = 25$).

	No.	%
Age		
Range	31–75 years	
Mean ± SD	54.4 ± 13.4	
Sex		
Male	16	64.0
Female	9	36.0
	Range (day)	Mean + SD
Duration of illness	10.0–90.0	31.3 + 7.7

Table 2 Etiological diagnosis of pleural effusion in the studied patients ($n = 25$).

Diagnosis	Number of patients (%)
Empyema	9 (36%)
Para pneumonic effusion	7 (28%)
Malignant effusion	6 (24%)
Tuberculous effusion	2 (8%)
Clotted haemothorax	1 (4%)

Table 3 Comparison between volumes of fluid drained before and after streptokinase instillation.

Amount of fluid drained	Mean	SD	Mean difference	95% CI	*P*. Value
Before streptokinase	246.8	151.6	1061.6	760.2–1363.0	< 0.001
After streptokinase	1308.4	799.9			

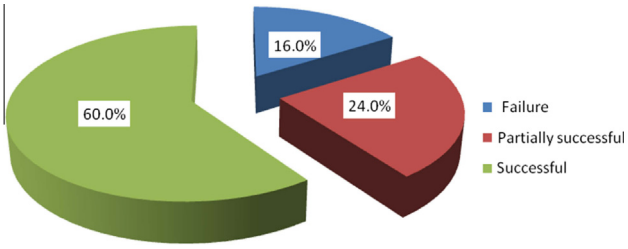


Figure 1 Outcome definitions of the studied patients.

Table 4 Total doses of streptokinase used in the studied patients.

Group	Total dose	
	Range (IU)	Mean + SD
Successful group (15)	1,250,000–3,000,000	1,650,000 + 35,232.5
Failure and partially successful group (10)	250,000–1,250,000	525,000 + 7.313

Table 5 Sonographic features of pleural adhesions among studied group.

Adhesions echo feature	Number of patients	Successful group	Partially successful and failure groups
Fine adhesions	10	10 (100%)	0
Coarse adhesions	8	1 (14%)	7 (86%)
Mixed	7	4 (57%)	3 (43%)

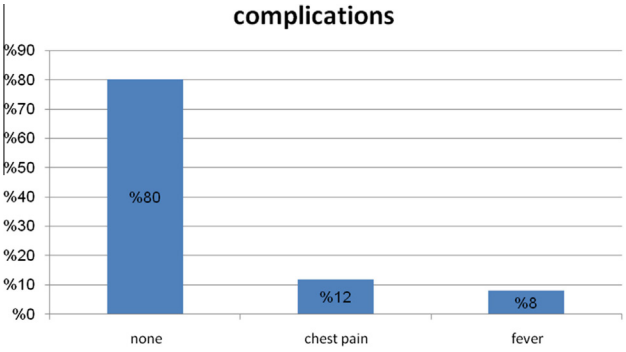


Figure 2 Complications in studied patients ($n = 25$).

The recorded complications in our study were only transient chest pain and fever in a few patients, while the majority recorded no complications Fig. 2.

Discussion

Tillet and Sherry first introduced fibrinolytic therapy in 1949 as a treatment for empyema and complicated parapneumonic effusion. Fibrinolytic therapy was reintroduced by Bergh et al. in 1977, using a more purified form of streptokinase. Since then, there have been many studies which support the use of fibrinolytic agents in empyema and parapneumonic effusion treatment. These agents may be a safer, easier and cost effective option for managing pleural adhesions and loculations [6]. This work is considered the first study in Assiut University Hospital about the therapeutic role of intrapleural fibrinolytics.

Our study included 25 patients presented by pleural effusion with intrapleural adhesions as documented by chest sonography. Their ages ranged from 31 to 75 years with the mean of 54.4 + 13.4. More than half of the studied patients were males (64% vs 36% females). In spite of the small number of patients included in our study, the commonest cases we faced were empyema and parapneumonic effusion (64%). This was comparable with Abu-Daff et al. in 2012 who used intrapleural fibrinolytics in 237 patients with loculated pleural effusion and about 68% of the cases were empyema and complicated parapneumonic effusion [6].

Regarding the amount of fluid drained before and after streptokinase instillation, our study reported marked difference between the two values with a mean value of 1061.6 with a significant statistical difference ($P < 0.001$).However, assessment of the response to intrapleural streptokinase in this work was based mainly on the changes that happened and detected in both chest X-ray and ultrasound after completing the course of therapy and on discharge. According to this rule, success (complete adhesiolysis) was recorded in 60% of cases and partial success in 24% while the procedure failed in 16% of cases. The percentage of success in our study (60%) was nearly similar to that reported by Temes et al.,1996 (61%) and approximate to that recorded by Taylor et al. in 1994 (67%).However, our success rate was lower than that seen in studies by Sanchez et al. in 1996 (92%) and Diacon et al. in 2004 (82%) [7–10]. We cannot exactly explain this variation in success rate, however experience, selection of cases and the parameters used to assess success; all may play a role.

In our work, sonographic examination was not only a helpful diagnostic tool but also it was valuable in predicting the patient outcome according to the echo features of pleural septa. In this study, we found that the chance of success was high when the adhesions or septa were fine. Previously, Chen et al. in 2000 use the sonographic septation as a useful prognostic indicator of acute thoracic empyema [11].

No major adverse effects were noted during application of the treatment protocol. Transient chest pain and fever were the only recorded complications in our study in a few patients. Taylor et al. in 1994 reported that all patients tolerated intrapleural streptokinase well; only one complained of mild chest discomfort shortly after each streptokinase instillation [8].

Conclusion and recommendation

We conclude that intrapleural streptokinase therapy may be considered in septated pleural effusion as a safe and effective treatment; it may obviate the need for surgery. Also, the ultrasound echo features of adhesions could be considered as a predictor for the response. Further trials using streptokinase and other fibrinolytic agents are recommended with a large number of patients (preferably multicenter controlled trials).

References

[1] P.C. Yang, K.T. Luh, D.B. Chang, et al, Value of sonography in determining the nature of pleural effusion: analysis of 320 cases, AJR 159 (1992) 29.
[2] S. Bielsa, J.M. Juan, J.M. Porcel, et al, Diagnostic and prognostic implications of pleural adhesions in malignant effusions, J. Thorac. Oncol. 3 (2008) 1251–1256.
[3] M.S. Barthwal, Intrapleural fibrinolytic therapy in complicated parapneumonic effusion and empyema: present status, Indian J. Chest Dis. Allied Sci. 50 (2008) 277–282.
[4] N.A. Maskell, C.W. Davies, A.J. Nunn, E.L. Hedley, F.V. Gleeson, R. Miller, U.K. controlled trial of intrapleural streptokinase for pleural infection, N. Engl. J. Med. 352 (9) (2005) 865–874.
[5] S.H. Talib, G.R. Verma, M. Arshad, B.O. Tayade, A. Rafeeque, Utility of intrapleural streptokinase in management of chronic empyemas, JAPI 51 (2003).
[6] S. Abu-Daff, D.E. Maziak, D. Alshehab, et al, Intrapleural fibrinolytic therapy (IPFT) in loculated pleural effusions—analysis of predictors for failure of therapy and bleeding: a cohort study, BMJ Open 3 (2013) e001887.
[7] R.T. Temes, F. Follis, R.M. Kessler, et al, Intrapleural fibrinolytics in management of empyema thoracis, Chest 110 (1996) 102–106.

[8] R.F.H. Taylor, M.B. Rubens, M.C. Pearson, et al, Intrapleural streptokinase in the management of empyema, Thorax 49 (1994) 856–859.
[9] J. Sanchez, A.R. Rivera, J.J. Eliazalde, R. Delado, et al, Intrapleural fibrinolysis with streptokinase as an adjunctive treatment in hemothorax and empyema, Chest 109 (1996) 1514–1519.
[10] A.H. Diacon, J. Theron, M.M. Schuurmans, B.W. van de Wal, C.T. Bolliger, Intrapleural streptokinase for empyema and complicated parapneumonic effusions, Am. J. Respir. Crit. Care Med. 170 (2004) 49–53.
[11] K.Y. Chen, Y.S. Liaw, H.C. Wang, K.T. Luh, P.C. Yang, Sonographic septation: a useful prognostic indicator of acute thoracic empyema, J. Ultrasound Med. 19 (12) (2000) 837–843.